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EXAMINER

HADDAD, MAHER M

ART UNIT PAPER NUMBER

1644

DATE MAILED: 10/22/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/051,168

Applicant(s)

NIESWANDT, BERNHARD

Examiner

Maher M. Haddad

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 July 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 7,8,15 and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 9-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

1. Claims 1-16 are pending.
2. Applicant's election with traverse of Group I, claims 1-6 and 9-14, filed on 7-24-02, is acknowledged.

Applicant's traversal is on the grounds that the Examiner fail to show a serious burden exists in searching Groups I-IV, wherein Groups II-IV have same classification and the product (Group I) and methods (Group II-IV) read on an antibody JAQ1. Furthermore, Group II is drawn to a method using a solid carrier "on which antibody JAQ1 is fixed" and Group [III] IV is drawn to a method comprising fixing "monoclonal antibody JAQ1 on a solid carrier". This is not found persuasive because the methods recited in Groups II-IV have different method steps therefore each method is patentably distinct. Therefore the product and the methods for the determination of the expression rate of collagen receptor GPVI in blood of a patient are distinct and independent, and searches of all groups would place an undue burden upon the examiner due to the distinct subject matter of each Group.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 7-8 and 15-16 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.
4. Claims 1-6 and 9-14 are under examination.

5. The use of the trademarks "ROMPUN®" and "IMALGEN 100®" have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-5 and 11-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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- A) Claims 1-5 and 11-13 are indefinite in the recitation of "active principle" since a principle is not an art recognize term and further the phrase refers to a chemical ingredient rather than a biological ingredient that exhibits or imparts a characteristic quality.
- B) Claim 1, line 3 is indefinite in the recitation of "degradation" it is unclear as how the active principle would degrade the collagen receptor and whether the active principle has an proleolytic activity.
- C) Claims 3, 5, 10 and 13-14 are indefinite in the recitation of "JAQ1" because its characteristics are not known. The use of "JAQ1" monoclonal antibody as the sole means of identifying the claimed antibody and hybridoma renders the claim indefinite because "JAQ1" is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation to define completely distinct hybridomas or cell lines. It is suggested that the DSM ACC 2487 be cited in the claims.
- D) It is improper to recite "Monoclonal antibody" in claim 10, line 1. It is suggested that the article "A" should be inserted before the phrase.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 3, 5, 9-10 and 13-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the **hybridoma DSM ACC 2487 that produce the JAQ1 antibody** is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, a deposit of the **hybridoma**, which produces this antibody, may satisfy first paragraph. See 37 CFR 1.801-1.809.

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the **hybridoma** has been deposited under the Budapest Treaty and that the **hybridoma** will be irrevocably and without restriction or condition released to

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the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample *or for the enforceable life of the patent whichever is longer*. See 37 CFR 1.806.

Further, amendment of the specification to disclose the date of deposit and the complete address of the depository is required as set forth in 37 C.F.R. 1.809(d).

10. Claims 1-5 and 10-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the JAQ1 antibody which specifically binds GPVI for diagnostic assays, does not reasonably provide enablement for **any medicament** for protection against thrombotic diseases, comprising at least one **active principle** that induces an irreversible inactivation or degradation of any **collagen receptor on thrombocytes** in claim 1; wherein the at least one active principle is **any antibody** in claim 2, wherein the at least one active principle is monoclonal antibody JAQ1 in claim 3, wherein the at least one active principle is humanized monoclonal antibody JAQ1 in claim 5, wherein the collagen receptor on thrombocytes is GPVI in claim 4; **any monoclonal antibody** that binds to the same or a similar epitope of **any collagen receptor** for thrombocytes as monoclonal antibody JAQ1 in claim 10; a method of producing **any medicament** against thrombotic diseases comprising providing at least one **active principle** that induces an irreversible inactivation or degradation of **any collagen receptor** on thrombocytes in claim 11, wherein the at least one active principle is **any monoclonal antibody** in claim 12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There is insufficient guidance and direction as to make and use medicaments comprising "at least active principle" that induces an irreversible inactivation or degradation of any "collagen receptor on thrombocytes", wherein the at least one active principle is "any antibody"; any monoclonal antibody that binds to the same or a similar epitope of any "collagen receptor" for thrombocytes as monoclonal antibody JAQ1.

Applicant has not provided sufficient biochemical information that distinctly identifies such "active principle" other than monoclonal JAQ1 antibody against GPVI. While any "active principle" may have some notion of the activity of the "inducing agent", claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such active principles, commensurate in scope with the claimed invention. The specification (page 5 under Antibodies, lines 5-19) fails to provide any guidance on how to make any medicament, any antibody, any collagen receptor, any GPVI epitope, or any monoclonal antibody or any polyclonal

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antibody that can be used to use to induce an irreversible inactivation or degradation of collagen receptor GPVI on thrombocytes.

There is insufficient guidance as to which amino acid segments within the collagen receptor GPVI can be unique and retain a distinct functional capability of the full length polypeptide. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since no epitope of a collagen receptor is mapped, an undue experimentation would be required to determine the epitope and any antibody that binds to the same or similar epitope of the collagen receptor. Further, the amino acid sequence of a polypeptide determined its structural property, predictability of which amino acid fragment can retain the functional capabilities of the full length polypeptide requires knowledge of, and guidance with regard to, which segments in the polypeptide's sequence contribute to its function.

Minor structural differences among structurally related compounds or compositions can result in substantially different biological activities. Therefore, structurally unrelated compounds comprising any "active principle" would be expected to have greater differences in their activities.

Because of this lack of guidance, an undue experimentation would be required to determine which modifications would be acceptable to retain occluding structural and functional activity, and the fact that the relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo *et al* in the Protein Folding problem and Tertiary Structure prediction, 1994, Merz *et al.*, (ed), Birkhauser, Boston, MA, pp.433 and 492-495), it would require an undue amount of experimentation for one of skill in the art to arrive at the claimed immunogenic epitopes of GPVI collagen receptor encompassed by the claimed invention

Also, at issue is whether or not the claimed medicament would function to protect "against thrombotic diseases". The specification discloses the treatment with monoclonal antibody JAQ1 resulted in profound long-term antithrombotic protection against collagen-dependent thromboembolism. The exemplification is drawn to the depletion of an activating glycoprotein receptor from circulation platelets, in a model of lethal pulmonary thromboembolism induced by infusion of a mixture of collagen and epinephrine (page 11).

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since mice animals were used as model system to protect against thrombotic disease. It is not clear that reliance on a model of lethal pulmonary thromboembolism induced by infusion of a mixture of collagen and epinephrine accurately reflects the relative mammal efficacy of the claimed therapeutic strategy. The specification does not adequately teach how to effectively reach any therapeutic

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endpoint in mammals by administering the therapeutic medicament. The specification does not teach how to extrapolate data obtained from a mice model of lethal pulmonary thromboembolism studies to the development of effective in vivo mammalian therapeutic protection, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the medicament exemplified in the specification.

However, an effective protocol for the protection against thrombotic diseases in mammalian is subject to a number of factors which enter the picture beyond simply the administration of the medicament in an acceptable formulation. Demonstrating depletion of an activating glycoprotein receptor from circulation platelets cannot alone support the predictability of the method for protection against thrombotic diseases through administration of the appropriate formulation. The ability of a host to suppress and thereby protect against thrombotic diseases will vary depending upon factors such as the condition of the host and burden of disease.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

11. Claims 1-5 and 10-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of JAQ1 antibody which specifically binds GPVI for diagnostic assays.

Applicant is not in possession of any medicament for protection against thrombotic diseases, comprising at least one active principle that induces an irreversible inactivation or degradation of any collagen receptor on thrombocytes in claim 1; wherein the at least one active principle is any antibody in claim 2, wherein the at least one active principle is monoclonal antibody JAQ1 in claim 3, wherein the at least one active principle is humanized monoclonal antibody JAQ1 in claim 5, wherein the collagen receptor on thrombocytes is GPVI in claim 4; any monoclonal antibody that binds to the same or a similar epitope of any collagen receptor for thrombocytes as monoclonal antibody JAQ1 in claim 10; a method of producing any medicament against thrombotic diseases comprising providing at least one active principle that induces an irreversible inactivation or degradation of any collagen receptor on thrombocytes in claim 11, wherein the at least one active principle is any monoclonal antibody in claim 12.

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Applicant has disclosed only JAQ1 antibody which specifically binds to collagen receptor GPVI; therefore, the skilled artisan cannot envision all the contemplated antibodies possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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13. Claims 1-4 and 9-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Nieswandt *et al* (IDS ref No. 7) (J Biol Chem. 275(31):23998-4002, 2000).

Nieswandt *et al* teach a medicament comprising a monoclonal antibody against the platelet collagen receptor glycoprotein GPVI (JAQ1) which inhibited collagen-induced platelet aggregation (see abstract and page 23400, right column, 2nd paragraph in particular). Finally Nieswandt *et al* teach a method for producing a monoclonal antibody and a hybridoma cell line for the production of the monoclonal antibody wherein the antibody is the monoclonal antibody JAQ1 (page 23999 under Production of Monoclonal antibodies in particular). While the prior art teachings may be silent as to the “induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes” per se; the antibody used in the reference is the same as the claimed antibody. Therefore “induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes” is considered inherent properties.

Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibody does not induce an irreversible inactivation or degradation of a collagen receptor on thrombocytes recited in the claim. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

The reference teachings anticipate the claimed invention.

14. Claims 1-2, 4 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Clemetson *et al* (IDS ref No. 6) (J Biol Chem. 274(41):29019-24, 1999).

Clemetson *et al* teach a medicament, comprising polyclonal antibodies fragment Fab against human platelet collagen receptor GPVI, which inhibited collagen-induced platelet aggregation (see abstract page 29019 and page 29021 1st paragraph in particular). Furthermore, Clemetson *et al* teach a method of producing the medicament, comprising preparing the polyclonal antibodies against human GPVI in rabbits and preparing Fab fragments using standard protocol (see page 29020 under Preparation of anti-GPVI Fab and Fa(ab')₂ in particular). While the prior art teachings may be silent as to the “induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes” per se; the antibody used in the reference is the same as the claimed antibody. Therefore “induces an irreversible inactivation or degradation of a collagen receptor on thrombocytes” is considered inherent properties.

Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibody does not induce an irreversible inactivation or degradation of a collagen receptor on thrombocytes recited in the claim. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

The reference teachings anticipate the claimed invention.

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15. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Buchanan *et al* (Thrombosis Research 29:125-1983).

Buchanan *et al* teach a medicament for protection against thrombotic diseases, comprising aspirin, which inhibited collagen-induced platelet aggregation (see abstract page 125 in particular).

Since the office does not have a laboratory to test the reference aspirin, it is applicant's burden to show that the reference aspirin does not induce an irreversible inactivation or degradation of a collagen receptor on thrombocytes recited in the claim. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

The reference teachings anticipate the claimed invention.

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nieswandt *et al*, in view of Owens *et al* (1994).

The teachings of Nieswandt *et al* reference have been discussed, *supra*.

The claimed invention differs from the reference teaching only by the recitation of a humanized antibody in claim 5.

Owens *et al* teach the modification of murine antibodies such as humanized antibody antibodies. Owens *et al* further teach humanized antibodies use in therapy of human diseases or disorders, since the human or humanized antibodies are much less likely to induce an immune response. (see the entire document).

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Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the monoclonal antibody taught by Nieswandt *et al* as humanized antibody as taught by the Owens *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the humanized antibodies are used in therapy of human diseases or disorders and much less likely to induce an immune response as taught by Owens *et al*.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nieswandt *et al* or Clemetson *et al* in view of U.S. Patent No. 6,406,888.

The teachings of Nieswandt *et al* or Clemetson *et al* have been discussed, *supra*.

The claimed invention differs from the reference teachings only by the recitation of a diagnostic agent comprising at least one labeled antibody chosen from a monoclonal antibody and a polyclonal antibody, wherein the at least one labeled antibody is directed against a GPVI epitope in claim 6

The '888 patent teaches antibodies that can be linked to other compounds, including therapeutic and diagnostic agents, using known methods to provide for targeting of those compounds to cells. For certain applications, including in vitro and in vivo diagnostic uses, it is advantageous to employ labeled antibodies. Suitable direct tags or labels include radionuclides, enzymes, substrates, cofactors, inhibitors, fluorescent markers, chemiluminescent markers, magnetic particles and the like; indirect tags or labels may feature use of biotin-avidin or other complement/anti-complement pairs as intermediates (column 28, line 26-36 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to label the polyclonal antibody taught by Clemetson *et al* or the monoclonal antibody taught by Nieswandt *et al* and use it as a diagnostic agent as taught by the '888 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because such labeled antibodies can be used in known methods for targeting specific compounds to cells.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at

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the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

19. Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clemetson *et al* (IDS ref No. 6) in view of in view of Harlow (1989).

The teachings of Clemetson *et al* reference have been discussed, *supra*.

The claimed invention differs from the reference teaching only by the recitation of a method of producing a medicament against thrombotic diseases comprising providing at least one active principle, wherein the at least one active principle is a monoclonal antibody.

Harlow *et al* teach a method of producing monoclonal antibodies comprising immunizing an animal (i.e. a mouse) with a protein or portion thereof (i.e. fragments), harvesting spleen cells from said animal, fusing said spleen cells with myeloma cell line, and culturing said fused cells (i.e hybridoma) under conditions that allow production of said antibody. Harlow *et al* further teach that the monoclonal antibodies stems from their specificity, homogeneity and ability to be produced in unlimited quantities (see pages 141-157 in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce monoclonal antibody using the method taught by Harlow *et al* with the immunogenic fragment taught by Clemetson *et al*.

One ordinary skill in the art at the time the invention was made would have been motivated to do so because the monoclonal antibodies produced exhibit a high degree of specificity and great affinity as taught by Harlow.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

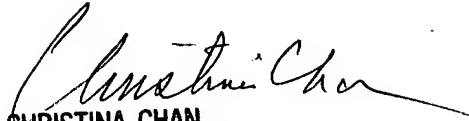
20. No claim is allowed.

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21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
October 21, 2002


CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600